REMARKS

Applicants request that the above amendment be entered in the instant application prior to substantive examination.

By the foregoing amendment to the specification, a cross-reference to the parent international application has been provided.

In addition, the amendment to claims 3, 10, 11, 13, 21, and 24 are presented in order to remove multiple dependencies. A marked up version of these amendments is presented attached herewith as Appendix A. Claims 26 and 27 are new and are the same as claims 26 and 27 attached as an Appendix to the IPER in the international application. Claims 28-37 are new and are fully supported by the application as filed. The attached application fee takes into consideration the aforementioned claim amendments and additions.

In light of the above amendments and additions, the claims presented for examination in the instant application are claims 1-37 (a clean copy of these claims is attached as Appendix B, for the Examiner's convenience). Applicants believe the presented claims are in condition for allowance and respectfully request an early indication of such favorable outcome.

Respectfully submitted,

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APPENDIX A
Marked-Up Version of Amendments Made Herein

In the specification:
Please replace the first paragraph of the specification with the following rewritten paragraph:

--This application claims priority from US provisional application 60/131,983 filed April 30 1999, whose contents are hereby incorporated by reference in their entirety. Further, this is application is a continuation of International Application No. PCT/EP98/00533 filed February 2, 1998, the entire disclosure of which is incorporated herein by reference.--

In the Claims:

3. (AMENDED) A specific binding member according to claim 1 [or 2] which comprises a CDR1 sequence substantially as set out as the CS37 VH CDR1 (SEQ ID NO: 11) and CS37 VH CDR2 (SEQ ID NO: 12).

10. (AMENDED) The isolated specific binding member of [any one of the preceding claims] claim 1 in the form of a single chain Fv (scFv).

11. (AMENDED) The isolated specific binding member of [any one of claims 1 to 9] claim 11 in the form of an IgG.

13. (AMENDED) A pharmaceutical composition comprising the specific binding member of [any one of the preceding claims] claim 1 in association with a pharmaceutically acceptable excipient, carrier, buffer or stabiliser.

21. (AMENDED) A method of treating a condition in a patient, the condition being associated with expression of $TGF\beta_1$, which comprises administering to said patient a specific binding member of [any one of claims 1 to 12 or a composition according to claim 13] claim 1.

23. (AMENDED) A method of determining the amount of TGFß1 in a sample which comprises bringing the sample into contact with a specific binding member according

to [any one of claims 1 to 12] claim 1, and determining the amount of binding of the specific binding member to TGFß1 in the sample.

24. (AMENDED) An isolated nucleic acid comprising a sequence which encodes the specific binding member of [any one of claims 1 to 12] claim 1.

Please Add the Following New Claims

26. A method for obtaining an antibody antigen binding domain specific for $TGF\beta_1$, the method comprising

providing by way of addition, deletion, substitution or insertion of one or more amino acids in the amino acid sequence of VH domain selected from SEQ ID NO. 4 and SEQ ID NO. 10 a VH domain which is an amino acid sequence variant of the VH domain, and combining the VH domain thus provided with one or more VL domains to provide one or more VH/VL combinations; and/or

providing by way of addition, deletion, substitution or insertion of one or more amino acids in the amino acid sequence of a VL domain selected from SEQ ID NO. 6 and SEQ ID NO. 8 a VL domain which is an amino acid sequence variant of the VL domain, and combining the VL domain thus provided with one or more VH domains to provide one or more VH/VL combinations; and

testing the VH/VL combination or combinations to identify an antibody antigen binding domain specific for $TGF\beta_1$.

27. A method of preparing a specific binding member specific for $TGF\beta_1$, which method comprises:

providing a starting repertoire of nucleic acids encoding a VH domain which either include a CDR3 to be replaced or lack a CDR3 encoding region;

combining said repertoire with a donor nucleic acid encoding an amino acid sequence substantially as set out herein for SL15 or JT182 VH CDR3 such that said donor nucleic acid is inserted into the CDR3 region in the repertoire, so as to provide a product repertoire of nucleic acids encoding a VH domain; and/or

providing a starting repertoire of nucleic acids encoding a VL domain which either

include a CDR3 to be replaced or lack a CDR3 encoding region;

combining said repertoire with a donor nucleic acid encoding an amino acid sequence substantially as set out herein for SL15 or JT182 VL CDR3 such that said donor nucleic acid is inserted into the CDR3 region in the repertoire, so as to provide a product repertoire of nucleic acids encoding a VL domain; and

expressing the nucleic acids of said product repertoire;

selecting a specific binding member specific for TGFß$_1$; and

recovering said specific binding member or nucleic acid encoding it.

28. A method of treating a condition in a patient, the condition being associated with expression of TGFß$_1$, which comprises administering to said patient a specific binding member of claim 5.

29. A method of treating a condition in a patient, the condition being associated with expression of TGFß$_1$, which comprises administering to said patient a specific binding member of claim 6.

30. A method of treating a condition in a patient, the condition being associated with expression of TGFß$_1$, which comprises administering to said patient a specific binding member of claim 7.

31. A method of treating a condition in a patient, the condition being associated with expression of TGFß$_1$, which comprises administering to said patient a specific binding member of claim 8.

32. A method of treating a condition in a patient, the condition being associated with expression of TGFß$_1$, which comprises administering to said patient specific binding member of claim 9.

33. An isolated nucleic acid comprising a sequence which encodes the specific binding member of claim 5.

34. An isolated nucleic acid comprising a sequence which encodes the specific binding member of claim 6.

35. An isolated nucleic acid comprising a sequence which encodes the specific binding member of claim 7.

36. An isolated nucleic acid comprising a sequence which encodes the specific binding member of claim 8.

37. An isolated nucleic acid comprising a sequence which encodes the specific binding member of claim 9.